

What is claimed is:

1           1. A method of analyzing a target nucleic acid,  
2 comprising:

3           (a) providing an array of probes comprising a probe  
4 set comprising probes complementary to a reference sequence;

5           (b) hybridizing the target nucleic acid to the  
6 array of probes;

7           (c) determining the relative hybridization of the  
8 probes to the target nucleic acid,

9           (d) estimating the sequence of the target nucleic  
10 acid from the relative hybridization of the probes;

11           (e) providing a further array of probes comprising  
12 a probe set comprising probes complementary to the estimated  
13 sequence of the target nucleic acid;

14           (f) hybridizing the target nucleic acid to the  
15 further array of probes;

16           (g) determining the relative hybridization of the  
17 probes to the target nucleic acid;

18           (h) reestimating the sequence of the target nucleic  
19 acid from the relative hybridization of the probes.

1           2. The method of claim 1, further comprising  
2 repeating steps (e)-(h) as necessary until the reestimated  
3 sequence of the target nucleic acid is the true sequence of  
4 the target nucleic acid.

1           3. The method of claim 1, wherein the target  
2 nucleic acid is a species variant of the reference sequence.

1           4. The method of claim 1, wherein the reference  
2 sequence is from a human and the target nucleic acid is from a  
3 primate.

1           5. The method of claim 1, wherein the target  
2 nucleic acid shows 50-99% sequence identity with the reference  
3 sequence.

1           6. The method of claim 1, wherein the target  
2 nucleic acid shows 80-95% sequence identity with the reference  
3 sequence.

1           7. The method of claim 1, wherein the reference  
2 sequence is at least 1000 nucleotides long, the array  
3 comprises a probe set comprising overlapping probes that are  
4 perfectly complementary to and span the reference sequence,  
5 and the further array comprises probes that are perfectly  
6 complementary to and span the estimated sequence.

1           8. The method of claim 1, wherein an estimated  
2 sequence of the target nucleic acid includes a position of  
3 ambiguity and the probe set showing perfect complementarity to  
4 the estimated sequence includes a probe having including a  
5 pooled nucleotide aligned with the position of ambiguity in  
6 the target sequence.

1           9. The method of claim 1, wherein the reference  
2 sequence is at least 10 kb.

1           10. The method of claim 1, wherein the reference  
2 sequence is at least 1000 kb.

1           11. The method of claim 1, wherein the reference  
2 sequence includes at least 90% of the human genome.

1           12. The method of claim 1, wherein the array of  
2 probes comprises:

3           (1) a first probe set comprising a plurality of  
4 probes, each probe comprising a segment of at least six  
5 nucleotides exactly complementary to a subsequence of the  
6 reference sequence, the segment including at least one  
7 interrogation position complementary to a corresponding  
8 nucleotide in the reference sequence,

9           (2) second, third and fourth probe sets, each  
10 comprising a corresponding probe for each probe in the first  
11 probe set, the probes in the second, third and fourth probe

12 sets being identical to a sequence comprising the  
13 corresponding probe from the first probe set or a subsequence  
14 of at least six nucleotides thereof that includes the at least  
15 one interrogation position, except that the at least one  
16 interrogation position is occupied by a different nucleotide  
17 in each of the four corresponding probes from the four probe  
18 sets.

1 13. The method of claim 12, wherein the sequence of  
2 the target nucleic acid is estimated by:

3 (a) comparing the relative specific binding of four  
4 corresponding probes from the first, second, third and fourth  
5 probe sets;

6 (b) assigning a nucleotide in the sequence of the  
7 target nucleic acid as the complement of the interrogation  
8 position of the probe having the greatest specific binding;

9 (c) repeating (a) and (b) until each nucleotide of  
10 interest in the sequence of the target nucleic acid has been  
11 estimated.

1 14. The method of claim 1, wherein the sequence of  
2 the target nucleic acid differs from the reference by at least  
3 two positions within a probe length.

1 15. A method of analyzing a target nucleic acid,  
2 comprising:

3 (a) designing an array of probes to be  
4 complementary to an estimated sequence of the target nucleic  
5 acid,

6 (b) hybridizing the array of probes to the target  
7 nucleic acid;

8 (c) determining a reestimated sequence of the  
9 target nucleic acid from the hybridization pattern of the  
10 array to the target nucleic acid sequence to; and

11 (d) repeating (a)-(c) at least once.